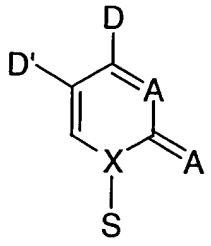
WHAT IS CLAIMED IS:

1. An immunostimulatory oligonucleotide compound, comprising an immunostimulatory dinucleotide of formula 5'-pyrimidine-purine-3', wherein pyrimidine is a non-natural pyrimidine nucleoside and purine is a natural or non-natural purine nucleoside.

2. An immunostimulatory oligonucleotide compound, comprising an immunostimulatory dinucleotide of formula C*pG, wherein C* is a cytidine analog, G is guanosine, 2'-deoxyguanosine, or a guanosine analog, and p is an internucleotide linkage selected from the group consisting of phosphodiester, phosphorothioate, and phosphorodithioate.

3. The immunostimulatory oligonucleotide compound of claim 1, wherein the non-natural pyrimidine nucleoside has the formula (*I*):



(*I*)

wherein D is a hydrogen bond donor, D' is selected from the group consisting of hydrogen, hydrogen bond donor, hydrogen bond acceptor, hydrophilic group, hydrophobic group, electron withdrawing group and electron donating group, A is a hydrogen bond acceptor or a hydrophilic group, X is carbon or nitrogen, and S is a pentose or hexose sugar ring, provided that the pyrimidine nucleoside of formula (*I*) is not cytidine or deoxycytidine.

4. The immunostimulatory oligonucleotide compound of claim 3, wherein the non-natural pyrimidine nucleoside includes a non-naturally occurring pyrimidine base.

5. The immunostimulatory oligonucleotide compound of claim 4, wherein the non-naturally occurring pyrimidine base is selected from the group consisting of 5-hydroxycytosine, 5-hydroxymethylcytosine, N4-alkylcytosine, and 4-thiouracil.

6. The immunostimulatory oligonucleotide compound of claim 4, wherein the non-naturally occurring pyrimidine base is selected from the group consisting of 5-hydroxycytosine and N4-ethylcytosine.

7. The immunostimulatory oligonucleotide compound of claim 4, wherein the non-natural pyrimidine nucleoside of formula (*I*) comprises a non-naturally occurring sugar moiety.

8. The immunostimulatory oligonucleotide compound of claim 7, wherein the non-naturally occurring sugar moiety is arabinose.

9. An immunostimulatory oligonucleotide compound comprising an immunostimulatory domain of formula (*II*):

5'------X1-X2-Y-Z-X3-X4------3' (*II*)

wherein

Y is cytidine, 2'-deoxycytidine, or a non-natural pyrimidine nucleoside;

Z is guanosine, 2'-deoxyguanosine, or a non-natural purine nucleoside;

X1 is a naturally occurring nucleoside or an immunostimulatory moiety selected from the group consisting of C3-alkyl linker, 2-aminobutyl-1,3-propanediol linker, and β-L-deoxynucleoside;

X2 is a naturally occurring nucleoside or an immunostimulatory moiety that is an amino linker;

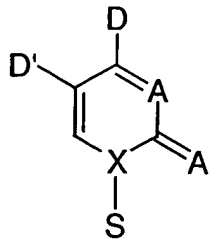
X3 is a naturally occurring nucleoside an immunostimulatory moiety that is a nucleoside methylphosphonate;

X4 is a naturally occurring nucleoside an immunostimulatory moiety selected from the group consisting of nucleoside methylphosphonate and 2'-O-methyl-ribonucleoside;

provided that at least one of X1, X2, X3, and X4 is an immunostimulatory moiety.

10. The immunostimulatory oligonucleotide compound ~~of~~ claim 9, wherein Y is a non-natural pyrimidine nucleoside.

11. The immunostimulatory oligonucleotide compound of claim 10, wherein Y has the formula (*I*):



(*I*)

wherein D is a hydrogen bond donor, D' is selected from the group consisting of hydrogen, hydrogen bond donor, hydrogen bond acceptor, hydrophilic group, hydrophobic group, electron withdrawing group and electron donating group, A is a hydrogen bond acceptor or a hydrophilic group, X is carbon or nitrogen, and S is a pentose or hexose sugar ring, provided that Y is not cytidine or deoxycytidine.

12. An immunostimulatory oligonucleotide compound comprising a sequence of formula (*III*):

5'-U*m*.....U1-X1-X2-Y-Z-X3-X4-D1.....D*m*-3' (*III*)

wherein:

Y is a non-natural pyrimidine nucleoside;

Z is guanosine, 2'-deoxy-guanosine or a non-natural purine nucleoside;

each X independently is a naturally occurring nucleoside or an immunostimulatory moiety;

wherein U*m*-U1 represents an upstream potentiation domain, where each U independently is a naturally occurring nucleoside or an immunostimulatory moiety;

wherein D1-D*m* represents a downstream potentiation domain , where each D independently is a naturally occurring nucleoside or an immunostimulatory moiety; and

m, at each occurrence, represents a number from 0 to 30.

13. The immunostimulatory oligonucleotide compound of claim 12, wherein at least one X, U, or D is an immunostimulatory moiety.

14. The immunostimulatory oligonucleotide compound of claim 13, wherein:

X1 is a naturally occurring nucleoside or an immunostimulatory moiety selected from the group consisting of C3-alkyl linker, 2-aminobutyl-1,3-propanediol linker, and β-L-deoxynucleoside;

X2 is a naturally occurring nucleoside or an immunostimulatory moiety that is an amino linker;

X3 is a naturally occurring nucleoside an immunostimulatory moiety that is a nucleoside methylphosphonate;

X4 is a naturally occurring nucleoside an immunostimulatory moiety selected from the group consisting of nucleoside methylphosphonate and 2'-O-methyl-ribonucleoside;

U1 is a naturally occurring nucleoside an immunostimulatory moiety selected from the group consisting of 1',2'-dideoxyribose, C3-linker, and 2'-O-methyl-ribonucleoside;

U2 is a naturally occurring nucleoside an immunostimulatory moiety selected from the group consisting of 1',2'-dideoxyribose, C3-linker, Spacer 18, 3'-deoxy-nucleoside, nucleoside methylphosphonate, β-L-deoxynucleoside, and 2'-O-propargyl-ribonucleoside;

U3 is a naturally occurring nucleoside an immunostimulatory moiety selected from the group consisting of 1',2'-dideoxyribose, C3-linker, Spacer 9, Spacer 18, nucleoside methylphosphonate, and 2'-5' linkage;

D1 is a naturally occurring nucleoside an immunostimulatory moiety selected from the group consisting of 1',2'-dideoxyribose and nucleoside methylphosphonate;

D2 is a naturally occurring nucleoside an immunostimulatory moiety selected from the group consisting of 1',2'-dideoxyribose, C3-linker, Spacer 9, Spacer 18, 2-aminobutyl-1,3-propanediol linker, nucleoside methylphosphonate, and β-L-deoxynucleoside; and

D3 is a naturally occurring nucleoside an immunostimulatory moiety selected from the group consisting of 3'-deoxynucleoside, 2'-O-propargylribonucleoside; and 2'-5' linkage.

15. The immunostimulatory oligonucleotide compound of claim 13, wherein U2 and U3 are both the same immunostimulatory moiety selected from the group consisting of 1',2'-didoxyribose, C3-linker, or β-L-deoxynucleoside.

16. The immunostimulatory oligonucleotide compound of claim 13, wherein U3 and U4 are both the same immunostimulatory moiety selected from the group consisting of nucleoside methylphosphonate and 2'-O-methoxyethylribonucleoside.

17. The immunostimulatory oligonucleotide compound of claim 13, wherein U5 and U6 are both the same immunostimulatory moiety selected from the group consisting of 1',2'-dideoxyribose and C3-linker.

18. The immunostimulatory oligonucleotide compound of claim 13, wherein X1 and U3 are both 1',2'-dideoxyribose.

19. The immunostimulatory oligonucleotide compound of claim 13, wherein D2 and D3 are both the same immunostimulatory moiety selected from the group consisting of 1',2'-dideoxyribose and β-L-deoxynucleoside.

20. An immunostimulatory oligonucleotide compound, comprising:

an immunostimulatory dinucleotide of formula 5'-pyrimidine-purine-3', wherein pyrimidine is a natural or non-natural pyrimidine nucleoside and purine is a natural or non-natural purine nucleoside;

a 3'-3' linkage; and

one or two accessible 5' ends;

provided that the oligonucleotide is not complementary to the *gag* or *tat* gene of HIV-1.

21. The immunostimulatory oligonucleotide compound of claim 20, which oligonucleotide comprises two accessible 5' ends.

22. The immunostimulatory oligonucleotide compound of claim 20, wherein the immunostimulatory dinucleotide comprises a non-natural pyrimidine nucleoside.

23. A method for modulating the immunostimulatory effect of an immunostimulatory oligonucleotide compound, comprising introducing into the

immunostimulatory domain a dinucleotide analog that includes a non-naturally occurring pyrimidine base.

24. A method for modulating the immunostimulatory effect of an immunostimulatory oligonucleotide compound, comprising introducing into the immunostimulatory domain and/or potentiation domain an immunostimulatory moiety.

25. A method for modulating the immunostimulatory effect of an immunostimulatory oligonucleotide compound, comprising introducing into the oligonucleotide a 3'-3' linkage.

26. A method for generating an immune response in a patient, such method comprising administering to the patient an oligonucleotide analog immunostimulatory compound according to any one of claims 1, 2, 9, 12, and 20.

27. The method according to claim 26, wherein the oligonucleotide analog immunostimulatory compound is administered in combination with an antibiotic, antigen, allergen, vaccine, antibody, cytotoxic agent, antisense oligonucleotide, gene therapy vector, DNA vaccine, adjuvant, or combination thereof.

28. The method according to claim 26, wherein the immunostimulatory oligonucleotide compound is conjugated to an antigen or vaccine.

29. The method according to claim 28, wherein such conjugation is to the 3'-end of the oligonucleotide compound.

30. A method for therapeutically treating a patient having disease caused by a pathogen, such method comprising administering to the patient an immunostimulatory oligonucleotide compound according to any of claims 1, 2, 9, 12, and 20.

31. The method according to claim 30, wherein the pathogen is a virus.

32. The method according to claim 30, wherein the pathogen is a parasite.

33. The method according to claim 30, wherein the pathogen is a bacterium.

34. A method for treating a cancer patient, such method comprising administering to the patient an immunostimulatory oligonucleotide compound according to any of claims 1, 2, 9, 12, and 20.

35. The method according to claim 34, wherein the immunostimulatory oligonucleotide compound is administered in combination with a chemotherapeutic compound.

36. A method for treating an autoimmune disorder, such method comprising administering to the patient an oligonucleotide analog immunostimulatory compound according to any of claims 1, 2, 9, 12, and 20.

37. The method according to claim 36, wherein the autoimmune disorder is autoimmune asthma.

38. A method for treating airway inflammation or allergy, such method comprising administering to the patient an oligonucleotide analog immunostimulatory compound according to any of claims 1, 2, 9, 12, and 20.